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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
10/14/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/646,950	RINE ET AL.	
	Examiner	Art Unit	
	DELIA M. RAMIREZ	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,9,11,15,17 and 21-32* is/are pending in the application.

4a) Of the above claim(s) *15,17,25,26,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,9,11,21-24 and 27-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *alignments, revision history, UniProtKB entries O75844,Q80W54,P47154,Q9U1H8*.

DETAILED ACTION

Status of the Application

Claims 1, 5, 9, 11, 15, 17, 21-32 are pending.

Applicant's amendment of claims 1, 5, addition of claims 21-32, and amendments to the specification as submitted in a communication filed on 9/12/2007 are acknowledged.

New claims 21-24 and 27-30 are deemed directed to the elected invention, i.e., Group A as indicated in the Non Final action of 9/26/2006. New claims 25-26 and 31-32 are directed to a non-elected invention, i.e., Group B as indicated in the Non Final action of 9/26/2006 and Group VI as indicated in the restriction requirement of 3/8/2006. At this time, the elected product claims are not allowable. Therefore a restriction requirement between product and method claims can be properly maintained. This application contains claims 15, 17, 25-26, 31-32 drawn to an invention non-elected with traverse. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1, 5, 9, 11, 21-24, 27-30 are at issue and are being examined herein.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

1. The previous objections to the specification are hereby withdrawn by virtue of Applicant's amendments to the specification which update the current status of priority applications and correct the sequence identifiers to be consistent with the Sequence Listing.

2. The specification is objected to for the following reasons. Upon reviewing the specification, the sequence listing and the GenBank records, it has been found that 1) the sequence of EST Z43273 is not that shown in SEQ ID NO: 5 but that of SEQ ID NO: 6, and 2) the sequence of EST W14344 is not that

shown in SEQ ID NO: 6 but that of SEQ ID NO: 5. Thus, page 17, first paragraph, of the specification should be amended to indicate this fact. Appropriate correction is required.

Claim Objections

3. Claims 1 and 5 are objected to due to the recitation of "nucleic acid having the sequence of human EST…(SEQ ID NO: X)". ". To clearly indicate that the recited EST has the sequence in parentheses, it is suggested the term be amended to recite "nucleic acid having the sequence of SEQ ID NO: X (human/mouse EST…)". Appropriate correction is required.

4. Claims 1 and 5 are objected to due to for the following reasons. Upon reviewing the specification, the sequence listing and the GenBank records, it has been found that 1) the sequence of EST Z43273 is not that shown in SEQ ID NO: 5 but that of SEQ ID NO: 6, 2) the sequence of EST W14344 is not that shown in SEQ ID NO: 6 but that of SEQ ID NO: 5, and 3) EST W14344 is not a human EST as recited in claim 5 but a mouse EST. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1, 5, 9, 11 remain rejected and new claims 21-24, 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. The rejection made due to the recitation of the terms "Afc1" and "Rce1" has been discussed at length in the Non Final action mailed on 9/26/2006 as it relates to claims 1, 5, 9 and 11. It is now applied to new claims 21-24, 27-30 for the reasons of record and those set forth below. This is a new rejection as it relates to claims 21-24, 27-30 which is necessitated by amendment.

8. Applicant argues that the terms "Afc1" and "Rce1" are definite terms in the art for specific CAAX proteases. Applicant indicates that the term "Face-2" is just a known synonym for Rce1 and that Rce1 and Face-2 are the same protein. In support of this, Applicant provides a UniProtKB/Swiss-Prot printout of entry Q9Y256.

9. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection or avoid the rejection of new claims 21-24 and 27-30. The Examiner acknowledges that the term "Rce1" appears to be one of the many synonyms associated with the human protein called CAAX prenyl protease 2, as shown in applicant's submission. However, the terms "Afc1" and "Rce1" still remain indefinite for the following reasons. As written, the terms appear to be generic and not limited to a protein isolated from a specific organism. It is reiterated herein that the specification fails to disclose which are the structural/functional features which are unique to Afc1/Rce1 proteins that would allow one of skill in the art to clearly distinguish an Afc1 or Rce1 protein from other CAAX proteases. While it is clear from the specification and the art that there are two *S. cerevisiae* CAAX proteases called Afc1 and Rce1, using these terms as indicative of a particular function for proteins from other organisms can be unclear and confusing in view of the fact that proteins having the same function in two different organisms can have different names. For example, UniProtKB/Swiss-Prot entries O75844 and Q80W54 disclose CAAX prenyl proteases both labeled FACE1 having the EC number 3.4.24.84 from human and mouse, respectively, whereas UniProtKB/Swiss-Prot entry P47154 discloses a CAAX prenyl protease labeled Afc1 having the same EC number 3.4.24.84. UniProtKB/Swiss-Prot entries O75844 and Q80W54 do not list the term "Afc1" as a synonym for FACE1. Therefore, using the term "Afc1" would not allow one of skill in the art to determine if the human and mouse CAAX proteases having the EC number 3.4.24.84 are intended to be encompassed by the term "Afc1", or if the claims are limited to a single CAAX protease from *S. cerevisiae*, i.e., Afc1. Similarly, UniProtKB/Swiss-Prot entry Q9U1H8 discloses a CAAX prenyl protease labeled FACE2 from *Drosophila melanogaster* which does not list the

term "Rce1" as synonym for FACE2, whereas UniProtKB/Swiss-Prot entry Q9Y256 lists "Rce1" as one of the synonyms for the human protein labeled FACE2, thus making it unclear as to whether the *D. melanogaster* FACE2 CAAX protease is encompassed by the term "Rce1", or if the term is intended to include some proteins, such as the human FACE2 protein, and not others even if they have the same biological function as that of the *S. cerevisiae* Rce1 protein. If the latter is true, neither the specification nor the art provide any information as to which proteins are included and which ones are not. Therefore, for the reasons of record and those set forth above, one of skill in the art cannot reasonably apprise of the scope of the claims. For examination purposes, no patentable weight will be given to the terms "Afc1" and "Rce1". Correction is required.

10. Claims 1, 5, 9, 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This is a new rejection necessitated by amendment.

11. Claims 1 and 5 (claims 9, 11 dependent thereon) are indefinite in the recitation of "hybridizes under stringent conditions" because it is unclear which polynucleotide is being referred to in the absence of a statement indicating the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. In addition, the art does not recognize a single set of conditions as stringent and even the specification indicates that there are different degrees of stringency (page 6, line 35-page 7, line 9). For examination purposes, it will be assumed that the term "stringent conditions" reads "any hybridization conditions". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

12. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

13. Claims 1, 5, 9, 11 remain rejected and new claims 21-24, 27-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new rejection as it relates to new claims 21-24, 27-30 necessitated by amendment.

14. This rejection has been discussed at length in the Non Final action mailed on 9/26/2006. It is applied to new claims 21-24, 27-30 for the reasons of record and those set forth below.

15. Applicant argues that the genus of polynucleotides recited is circumscribed by both structure and function.

16. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection or avoid the rejection of new claims 21-24, 27-30. Claims 1, 5, 9, 11 are still directed to products that require a genus of polynucleotides encoding CAAX proteases wherein said polynucleotides hybridize under any conditions to the polynucleotides of SEQ ID NO: 5 or 6. New claims 21-24 and 27-30 are directed to products that require a genus of polynucleotides which comprise SEQ ID NO: 5 or 6, or a genus of polynucleotides which hybridize under specific conditions to the polynucleotides of SEQ ID NO: 5 or 6. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation. The Examiner acknowledges the amendments to the claims. However the genus of polynucleotides recited fail to meet the written description requirement for the following reasons.

The polynucleotides of SEQ ID NO: 5 (mouse) and 6 (human) are 373 and 362 nucleotides in length, respectively. These polynucleotides were first disclosed as ESTs in GenBank as having accession numbers Z43273 (human; available to the public on November 11, 1994) and W14344 (mouse; available to the public on April 26, 1996). See attached revision history for these entries. Thus, the polynucleotides of SEQ ID NO: 5 and 6 do not encode full-length CAAX proteases. The full length

human CAAX protease encoded by a polynucleotide which appears to comprise most of EST Z43273 was disclosed by Kumagai et al. (Biochim. Biophys. Acta 1426:468-474, 1999; protein, GenBank accession number O75844, 1999), and the full length mouse CAAX protease encoded by a polynucleotide which appears to comprise most of the EST W14344 was disclosed by Cadinanos et al. (protein, GenBank accession number CAC17013; November 2000). See attached alignments. While the specification discloses that the polynucleotides of SEQ ID NO: 5 and 6 can be used as probes to isolate polynucleotides which encode full length CAAX proteases, the specification fails to disclose the remaining structure of a polynucleotide encoding an entire CAAX protease, including mouse or human, nor does it provide a working example indicating the actual isolation of a mouse or human polynucleotide encoding a full-length CAAX protease.

In addition, an alignment of the ESTs shown in SEQ ID NO: 5 and 6 with the polynucleotides encoding the mouse and human polypeptides of Kumagai et al. (nucleic acid, GenBank accession number AB016068, 1998) and Cadinanos et al. (nucleic acid, GenBank accession number MMU251645, 2000; cited in the previous Office action) shows that (1) a polynucleotide comprising SEQ ID NO: 5 would not necessarily encode a protein having CAAX proteolytic activity or even a catalytically active fragment of the polypeptide of Cadinanos et al. in view of the fact that at position 256 of SEQ ID NO: 5 there is an indel of one nucleotide, and (2) a polynucleotide comprising SEQ ID NO: 6 would not necessarily encode a protein having CAAX proteolytic activity or even a catalytically active fragment of the protein of Kumagai et al. in view of the fact that at position 204 of SEQ ID NO: 6 there is an indel of one nucleotide. These indels would shift the reading frame such that it is unclear as to what polynucleotides comprising SEQ ID NO: 5 or 6 would actually encode or whether these polynucleotides would encode proteins having CAAX proteolytic activity.

It should be noted that even if EST W14344 (SEQ ID NO: 5) and EST Z43273 (SEQ ID NO: 6) were to encode a fragment of a CAAX protease, such fragment would be approximately 120 amino acids

in length (120 amino acids = 360/3; SEQ ID NO: 5 = 373 nucleotides; SEQ ID NO: 6 = 362 nucleotides). Since the mouse protein of Cadinanos et al. is 329 amino acids long and the protein of Kumagai et al. is 475 amino acids long, even if the polynucleotides of SEQ ID NO: 5 and 6 were fragments of the polynucleotides of Kumagai et al. and Cadinanos et al., the polynucleotides of SEQ ID NO: 5 and 6 would encode approximately one third of the mouse protein of Cadinanos et al. and one quarter of the human protein of Kumagai, respectively. As such, the polynucleotides of SEQ ID NO: 5 and 6 represent at best one third and one quarter of the coding region of the polynucleotides encoding the mouse and human CAAX proteins of Cadinanos et al. and Kumagai et al., respectively.

The specification fails to disclose a structure/function correlation which would allow one of skill in the art to envision (1) the complete structure of any polynucleotide which encodes a full length CAAX protease and hybridizes under any conditions or the conditions recited in claims 21-24 to the polynucleotides of SEQ ID NO: 5 or 6, or (2) the remaining two thirds or three quarters of the coding region of the mouse or human polynucleotides encoding the mouse or human CAAX proteases. No disclosure of the structural features required in the enormous genus of nucleic acids recited for these nucleic acids to encode a protein having CAAX protease activity has been provided either. As indicated in the Non Final action, the art clearly teaches that structural similarity does not always translate into functional similarity. Since nothing is known regarding how structure correlates with CAAX proteolytic activity and the art recognizes that even small structural modifications can result in unexpected functional variation, one cannot reasonably conclude that SEQ ID NO: 5 or 6 are representative of the structure of any polynucleotide as recited. In the instant case, not a single polynucleotide comprising SEQ ID NO: 5 or 6 that encodes a full-length CAAX protease (or enzymatically active fragment thereof) has been disclosed, let alone variants of the polynucleotides of SEQ ID NO: 5 or 6 as recited which encode full length CAAX proteases (or enzymatically active fragments thereof). Since not a single species of the

recited genus of nucleic acids have been provided, one cannot reasonably conclude that the claimed invention is adequately described by the teachings of the specification.

17. Claims 1, 5, 9, 11 remain rejected and new claims 21-24, 27-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a new rejection as it relates to new claims 21-24, 27-30 necessitated by amendment.

18. This rejection has been discussed at length in the Non Final action mailed on 9/26/2006. It is applied to new claims 21-24, 27-30 for the reasons of record and those set forth below.

19. Applicant argues that the genus of polynucleotides recited is circumscribed by both structure and function.

20. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection or avoid the rejection of new claims 21-24, 27-30. As indicated above, (1) claims 1, 5, 9, 11 are directed to products that require a genus of polynucleotides encoding CAAX proteases wherein said polynucleotides hybridize under any conditions to the polynucleotides of SEQ ID NO: 5 or 6, and (2) new claims 21-24 and 27-30 are directed to products that require a genus of polynucleotides which comprise SEQ ID NO: 5 or 6, or a genus of polynucleotides which hybridize under specific conditions to the polynucleotides of SEQ ID NO: 5 or 6. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation. The Examiner acknowledges the amendments to the claims. However the claimed invention fails to meet the enablement requirement for the following reasons.

As extensively discussed above, the polynucleotides of SEQ ID NO: 5 (mouse) and SEQ ID NO: 6 (human) are fragments of nucleic acids encoding CAAX proteases which were first disclosed in GenBank as ESTs having accession numbers W14344 (mouse) and Z43273 (human). These ESTs were

disclosed prior to the priority date of 8/7/2006. While there is a statement in the specification indicating that these ESTs can be used to isolate the full-length polynucleotides encoding the corresponding mouse and human CAAX proteases, neither the priority document nor the specification have disclosed the entire polynucleotide (or coding region) from which these ESTs derived, nor there is any indication that Applicant actually isolated the full-length polynucleotides (or coding polynucleotides) from which these ESTs derived. The full length human CAAX protease encoded by a polynucleotide which appears to comprise most of EST Z43273 was disclosed by Kumagai et al., and the full length mouse CAAX protease encoded by a polynucleotide which appears to comprise most of the EST W14344 was disclosed by Cadinanos et al. However, as previously indicated, the polynucleotides of SEQ ID NO: 5 and 6 do not appear to encode a CAAX protease or enzymatically active fragment thereof in view of the presence of indels in both polynucleotides which would cause a shift in the reading frame. As such, polynucleotides comprising SEQ ID NO: 5 or 6 would not be necessarily expected to encode a CAAX protease or even an enzymatically active fragment of the polypeptides of Kumagai et al. or Cadinanos et al.

The enablement provided in the specification is not commensurate in scope with the claims due to the extremely large number of proteins of essentially unknown structure encompassed by the claims and the fact that there is no indication that the polypeptides encoded by polynucleotides comprising SEQ ID NO: 5 or 6 would have CAAX protease activity. It is reiterated herein that the specification fails to provide (1) the critical structural features required in any variant of the polynucleotides of SEQ ID NO: 5 or 6 to encode a protein having the desired activity, (2) a structure/function correlation which would allow one of skill in the art to envision the structure of the polynucleotides required by the claims, or (3) the structural elements required by the recited polynucleotides in addition to SEQ ID NO: 5 or 6 which are necessary for a protein encoded by said polynucleotides to have CAAX protease activity.

In addition to polynucleotides comprising SEQ ID NO: 5 or 6, the claims encompass an essentially infinite number of variants of said polynucleotides. See Claim Rejections under 35 USC 112, second paragraph, for interpretation of claims 1, 5, 9 and 11. Furthermore, a calculation of the Tm of the polynucleotides recited in claims 21-24 shows that under the hybridization conditions recited, the recited polynucleotides can be approximately 86% sequence identical to the polynucleotides of SEQ ID NO: 5 or 6. Using the well known equation of Meinkoth and Wahl (Current Protocols in Molecular Biology, Hybridization Analysis of DNA Blots, pages 2.10.8-2.10.11, 1993), Tm = 81.5 ºC +16.6x$\log_{10}$[Na+] +0.41x(%GC) - .61x(%form) – 500/L, the corresponding Tm for the polynucleotide recited is approximately 79 ºC assuming a G+C content of 50% and neglecting the term 500/L (L=length of polynucleotide) (79 ºC = 81.5 + 16.6x$\log_{10}$[3.9/100] +0.41x(%50) - .61(%form = 0); for 20xSSC the molar concentration of Na+ is 3.9). As known in the art, Tm is reduced by approximately 1 ºC for each 1% mismatching, therefore under the wash conditions recited (0.2xSSC and 65 ºC), a wash at 65 ºC is equivalent to approximately 14% mismatching (14% = 79ºC – 65ºC). This level of mismatching amounts to 53 and 51 nucleotides which can be modified (53 = 0.14x373; 51 = 0.14x362) within SEQ ID NO: 5 and 6, respectively, wherein each of those modification can affect the same number of codons.

The total number of variants of a polynucleotide having a specific sequence identity can be calculated from the formula N!x3^{A}/(N-A)!/A!, where N is the length in nucleotides of the reference polynucleotide and A is the number of allowed substitutions for a specific % identity. Thus, for a variant of the polypeptide of SEQ ID NO: 5 having 86% sequence identity to SEQ ID NO: 5, the total number of variants to be tested is 373!x3^{53}/(373-53)!/53! (SEQ ID NO: 5 has 373 nucleotides; 53 nucleotides = 0.14x373) or 1.86x10^{90} variants. A similar calculation for variants having 86% sequence identity to SEQ ID NO: 6 yields 1.07x10^{87} variants. Since neither the specification nor the art have provided a rational scheme to determine which of the essentially infinite number of variants recited in the claims have structural features associated with the desired activity, one of skill in the art is left with the task of testing

an infinite number of variants and determine which ones encode a protein having CAAX protease activity. Similarly, since neither the specification nor the art have provided any information as to whether the polynucleotides of SEQ ID NO: 5 or 6 encode catalytically active proteins, or which additional structural features are required beyond SEQ ID NO: 5 or 6 to encode a CAAX protease, one of skill in the art is left with the task of testing an infinite number of polynucleotides comprising SEQ ID NO: 5 or 6 and determine which ones encode a CAAX protease. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, as is the case herein, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that a reasonable number of species can be selected for testing. In view of the fact that such guidance has not been provided in the instant specification, it would require undue experimentation to enable the full scope of the claims.

Art of Interest

21. As previously indicated in the Non Final action of 9/26/2006, Kikly et al. (U.S. Patent No. 6060277) discloses polynucleotides encoding a human CAAX protease comprising SEQ ID NO: 6 except for 4 mismatches. It should also be noted that U.S. Patent No. 6060277 claims nucleic acids which would fall within the genus of nucleic acids and cells claimed. See, for example, claims 5, 6 and 9 of said patent.

Conclusion

22. No claim is in condition for allowance.

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

24. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashaat Nashed can be reached on (571) 272-0934. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

/Delia M. Ramirez/

Delia M. Ramirez, Ph.D.
Primary Patent Examiner
Art Unit 1652

DR
October 10, 2008